UNIVERSITY HOSPITAL

Schmeckel

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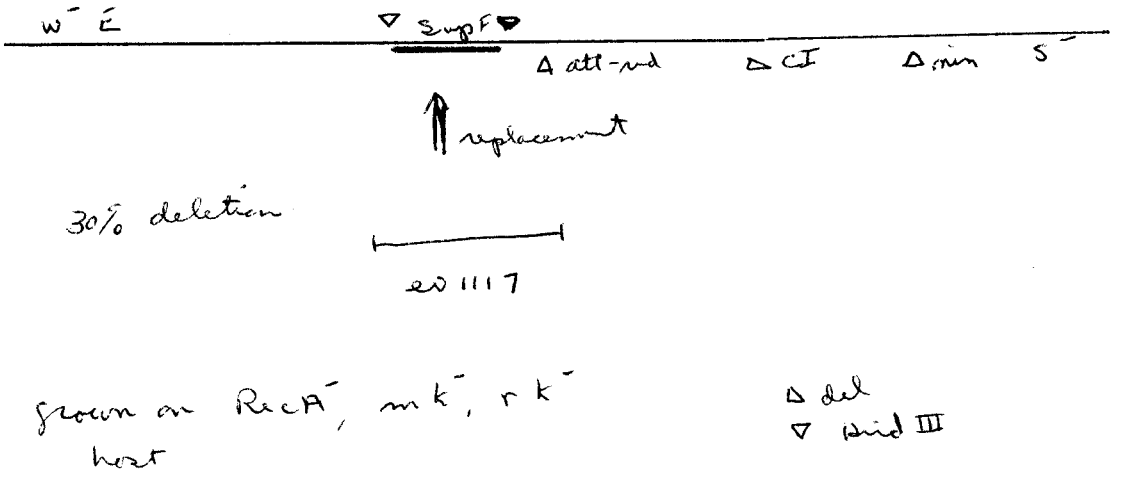
Dr. Daniel Nathans
Johns Hopkins University
Department of Microbiology
Wolfe Street
Baltimore, Maryland

Dear Dan:

I have finally arrived back in Ann Arbor after a very stimulating year. Unfortunately, the politics of recombinant DNA have put me in a holding pattern. As you recall, just before the Boston meeting, I wrote to you to tell you that we had put the SV40 into the left operator region of lambda. We prepared the DNA and were ready to do the translation experiments with the help of the reagents you sent over. However, during the Boston meeting which Noreen attended, the discussion of the vector that I had helped her prepare led her to feel uncertain in its use. As you may recall, the vector we had prepared had an amber mutation in the W gene, and another amber in the S gene. In addition, the lambda had deletions of att, red, immunity, and nin. They had been grown in m- and r- hosts. The only difference between our vector and the Enquist vector was that it had one more amber mutation (E) in the left arm. However, it did not have the cI deletion. For this reason, Noreen felt it was only right to start all over again and make the vector with the 3 amber mutations. To do that we had to start with a host that did not have the suppressor fragment in it and cross in an E mutation. After this was done, we did another *in vitro* recombination to put a suppressor fragment in the lambda as I have drawn below.



Although time was short, I then used the purified ev 117 and got another SV40-lambda recombinant. However, all of this was at the very end of my time in Edinburgh, and this left no time for testing out the new recombinant, and no time for doing any translation.

At present I am waiting to hear from Noreen to make sure that the new recombinant tests out, and that she has confidence that the new vector is correct. At the time that I did this work she was in Switzerland and I did not get a chance to talk to her before I left. So, after frantic work I just about got back to where I was when I wrote to you in June. This still leaves us without the chance to check translation.

I'm writing you just to catch you up on the news and not because I am clear on what to do next. My own inclination is to wait until Noreen gets in touch with me and is ready to send me the recombinant molecule that I made. I then imagine it will be necessary to clear the vector with the NIH advisory panel. If it clears, and I see no reason why it shouldn't clear, I think that you and I could discuss the best way to perform the translation experiments rapidly.

At the present time all of this is disappointing and I hope everything can be straightened out. I will get in touch with you as soon as I find out about my recombinant molecule and the state of the vector.

Again, thank you for your help, and I certainly hope that things will work out.

Sincerely yours,

Roy

Roy D. Schmickel, M.D.
Professor of Pediatric &
Comm. Diseases

RDS/dl

I may not have made it clear but the problem Noreen has is to show the E mutation is in the final vector because the Sup F fragment suppresses the amber mutations. What's more, it is a double Sup F mutation. Which goes to say that the more complicated a vector is, the more unsafe it is because of the difficulty in testing it safely.

RS